UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/754,711	01/12/2004	Deborah Kim Glencross	025455-113	1340

21839 7590 02/22/2006

BUCHANAN INGERSOLL PC
(INCLUDING BURNS, DOANE, SWECKER & MATHIS)
POST OFFICE BOX 1404
ALEXANDRIA, VA 22313-1404

EXAMINER	
FORD, ALLISON M	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 02/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/754,711	GLENCROSS, DEBORAH KIM	
	Examiner	Art Unit	
	Allison M. Ford	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *3,4 and 6-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5 and 14-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendments

Applicant's amendments filed 12 December 2005 to claims 1 and 2 have been entered. Claims 14-16 have been added. Claims 1-16 remain pending in the current application, with claims 3-4 and 6-13 being withdrawn from consideration. Claims 1, 2, 5, and 14-16 have been considered on the merits.

Specification

The new title is accepted by the examiner. The new title is: ENUMERATION OF CD4+ LYMPHOCYTES.

Priority

Acknowledgment is made of applicant's claim for priority as a continuation of PCT/IB/02/02725 filed on 11 July 2002, which further claims priority to South African application 2001/5700, filed on 11 July 2001.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 5 and 14-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant's claim 1 is directed to a method of enumerating the number of CD4+ lymphocytes in a cell sample, comprising a) identifying the total while blood cell population in a cell sample as a reference

population; b) determining the percentage of CD4+ lymphocytes as a function of the total white blood cell reference population; c) determining the number of white blood cells per volume of blood in the sample; and d) calculating the absolute number of CD4+ lymphocytes in the sample by multiplying the percentage of CD4+ lymphocytes obtained in step (b) by the white blood cell count obtained in step (c).

First, it is noted that it would be clearer if reference was made to a cell sample in step (a) of claim 1, this would make it clear that the cell sample referenced in step (b) is one and the same as that used in step (a).

It was previously noted that steps (a) and (c) appeared to be identical, as they both seemed to require identification of the number of white blood cells in a known volume of blood; however, applicants have traversed this rejection stating that step (a) merely requires counting the actual number of white blood cells present in the sample, without any acknowledgement of the sample volume, and step (c) requires a mental step of correlating the white blood cell count, obtained in (a), with the volume of the blood sample to obtain the number of white blood cells *per volume* of sample. While it is now understood how applicant is interpreting the determination as two distinct steps, step (c) is merely a mental step of noting the volume of the blood sample from which the white blood cells were counted. One of any level of skill in the art would automatically correlate the number of white blood cells counted to the volume of the sample to obtain the number of cells *per volume.* Reciting two separate steps actually renders the claim extremely confusing, as one of ordinary skill in the art would immediately envisage a step of counting the total number of white blood cells in a sample to include correlation to the sample volume to obtain the number of white blood cells per volume, and therefore would be confused as to what step (c) requires.

Claims 1, 2 and 16 are further indefinite because they do not clearly recite the action required to perform the steps. In claim 1, the recited steps include "identifying" and "determining" certain cell counts and percentages, however applicant fails to claim actual methods for performing such

'identification' and 'determination' steps. From the specification it appears step (a)/(c) of claim 1 are to involve identifying the total white blood cell population in a cell sample by means of a hematology analyzer. Claims 2 and 16 are directed to identification step (c) in claim 1, but they also fail to present any further limitation on how such identification is to be performed, specifically, claim 2 requires a 'single platform determination' of CD45+ cells, but does not recite any specific single platform method; claim 16 requires the CD45+ population to be identified, but provides no method to do such. Additionally, from the specification it appears that step (b) determining the percentage of CD4+ lymphocytes requires a specific flow cytometric assay involving specific gating strategies and calculation of CD4++ low side scatter lymphocytes (See Spec, Pg. 17); such specific steps must be recited in the claim as they are essential to the claimed method. Without clearly describing, in the claim, how the determination of the percentage of CD4+ cells is obtained, it is not clear if the claimed method is a single platform method or dual platform method, and thus cannot accurately be compared to such methods of the prior art.

Applicant's claim 14 fails to accurately and precisely define the method. It appears the claim is requiring the identification of the number of white blood cells to be performed using a bead based counting method on a flow cytometer, however, the claim fails to recite use of a flow cytometer and only states that beads are to be added to the cell sample and for the beads and cells to be counted. It is also noted that the specification teaches away from use of bead based counting, stating that it is especially prone to error introduced by errors of pipetting (See Spec Pg. 19, ln 29- Pg. 20, ln 1); therefore it is not clear why applicant is claiming a method they are denouncing in their specification.

Applicant's claim 15 is confusing because use of hematology analyzer to determine the total white blood cell count is not a dual platform determination, as claimed. Use of a hematology analyzer is a single step (a single platform) that may be part of a dual step (dual platform) method, wherein the

hematology analyzer is the first platform, and then subsequent analysis on a flow cytometer is the second platform.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2 and 15-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Melnicoff et al (US Patent 5,385,822), in light of Dorland's Illustrated Medical Dictionary, 2005.

The claims are directed to a method for enumerating the number of CD4 cells or subset thereof in a cell sample, the method comprising the steps of: a) identifying the total CD45 expressing population as a reference population; b) determining the percentage of CD4 positive lymphocytes or subset thereof as a function of the total CD45 expressing reference population identified in step (a); c) determining the number of CD4 positive cells per volume of blood; and d) calculating the number of CD4 positive cells or subset thereof in the sample by multiplying the percentage of CD4 positive cells, obtained in step (b), by the CD 45 expressing cell count obtained in step (c).

Melnicoff et al teach a method of enumerating the number of CD4+ lymphocytes in a blood cell sample, comprising identifying the total leukocyte (CD45+ white blood cell) population on a Coulter counter, to be used as a reference population; followed by labeling the cell samples with fluorescent markers against CD4 and CD45; then performing flow cytometry to determine the percent of leukocytes (CD45+) that are CD4+ lymphocytes; the percent CD4+ lymphocytes is then multiplied by the leukocyte count to determine the number of CD4+ lymphocytes/mm^3 blood (See col. 19, ln 15-col. 21, ln 50; especially Ex. 3a steps 7-8 & 16-17 and Ex. 3c step 11) (Claim 1).

Melnicoff et al initially count the number of leukocytes (CD45+) cells by means of a Coulter counter (See Col. 19, ln 51-52); a Coulter counter is a type of hematology analyzer that can be used to count the number of formed elements (such as leukocytes) in a cubic millimeter of blood (See Dorland's Medical Dictionary); therefore, Melnicoff et al determining the number of white blood cells (CD45+ cells) per volume of blood using a hematology analyzer (Claim 16). Use of a hematology analyzer constitutes a 'single platform' and thus is a single platform determination of CD45+ cells (Claim 2); however, applicants also refer to use of hematology analyzer to determine the number of white blood cells per volume of blood to be a dual platform determination, though it only utilizes one 'platform' (Claim 15). Therefore the reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2, 5, 14 & 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Melnicoff et al (US Patent 5,385,822), in view of Brando et al (Cytometry, 2000).

The claims are directed to a method for enumerating the number of CD4 cells or subset thereof in a cell sample, the method comprising the steps of: a) identifying the total CD45 expressing population as a reference population; b) determining the percentage of CD4 positive lymphocytes or subset thereof as a function of the total CD45 expressing reference population identified in step (a); c) determining the number of CD4 positive cells per volume of blood; and d) calculating the number of CD4 positive cells or subset thereof in the sample by multiplying the percentage of CD4 positive cells, obtained in step (b), by the CD 45 expressing cell count obtained in step (c).

Melnicoff et al teach a method of enumerating the number of CD4+ lymphocytes in a blood cell sample, comprising identifying the total leukocyte (CD45+ white blood cell) population on a Coulter counter, to be used as a reference population; followed by labeling the cell samples with fluorescent markers against CD4 and CD45; then performing flow cytometry to determine the percent of leukocytes (CD45+) that are CD4+ lymphocytes; the percent CD4+ lymphocytes is then multiplied by the leukocyte count to determine the number of CD4+ lymphocytes/mm^3 blood (See col. 19, ln 15-col. 21, ln 50; especially Ex. 3a steps 7-8 & 16-17 and Ex. 3c step 11).

Melnicoff et al initially count the number of leukocytes (CD45+) cells by means of a Coulter counter (See Col. 19, ln 51-52); a Coulter counter is a type of hematology analyzer that can be used to count the number of formed elements (such as leukocytes) in a cubic millimeter of blood (See Dorland's Medical Dictionary).

Additionally, though Melnicoff et al initially count the number of leukocytes (CD 45+ cells) by means of a Coulter counter it would have been obvious to one of ordinary skill in the art at the time the invention was made to alternatively use microbead-based technologies to count the number of leukocytes per volume of blood (See Brando et al, Pg. 334, col. 2- Pg. 335, col. 2) (Claims 14 &16).

It would further have been obvious to one of ordinary skill in the art to use any available blood sample to perform the analysis, including whole unlysed blood, unfractionated, fractionated or lysed whole blood (Claim 5). One of ordinary skill in the art would have been motivated to use any type of blood sample provided to perform the analysis because only the white blood cells are needed in the method. One of ordinary skill in the art would be motivated to use any type of blood sample in order to test the blood to monitor the progression of HIV in infected patients. Fractionating or lysing the blood sample would not affect the number of white blood cells or the CD4 or CD45 protein markers on the cells; therefore, one would expect success using any type of blood sample, based on what type of sample

was provided, because a skilled technician would be able to identify and isolate the white blood cells from any type of blood sample and perform the method of Melnicoff et al.

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1, 2, 5 and 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brando et al (Cytometry, 2000), in view of Barnett et al (British Journal of Haematology, 1999).

The claims are directed to a method for enumerating the number of CD4 cells or subset thereof in a cell sample, the method comprising the steps of: a) identifying the total CD45 expressing population as a reference population; b) determining the percentage of CD4 positive lymphocytes or subset thereof as a function of the total CD45 expressing reference population identified in step (a); c) determining the number of CD4 positive cells per volume of blood; and d) calculating the number of CD4 positive cells or subset thereof in the sample by multiplying the percentage of CD4 positive cells, obtained in step (b), by the CD 45 expressing cell count obtained in step (c).

Brando et al teach a dual platform method for enumerating the number of cells in a given cell subset, comprising using a hematology analyzer to determine the number of reference cells per volume of sample to obtain an absolute cell count of a reference cell population (first platform); utilizing flow cytometry to determine the percentage of cells of the chosen cell subset in a reference sample (% cells of interest/reference sample) (second platform); and then calculating the absolute cell count of the given cell subset as a function of the absolute cell count of the reference population (absolute cell count of cells of interest = (% of cells of interest/100%) x absolute cell count of reference cell population). Brando et al teach the total leukocyte population can be used as the reference population; the pan-leukocyte CD45 marker can be used in the gating strategy to encompass all leukocytes (Se pg. 329, col. 2- Pg. 330, col. 2).

Though Brando et al do not provide an example wherein CD4+ cells are the given cell subset in the dual platform method, they do exemplify CD4+ cells as the cell subset of interest in the single platform technique example. Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to enumerate CD4+ cells from a blood sample (as the given cell subset) in the method of Brando et al, wherein the total leukocyte population is used as the reference population and the number of CD45+ white blood cells per volume is first determined on a hematology analyzer (such counting method by itself is a 'single platform method,' but applicant also calls this method a dual platform method), and then the percentage of CD4+ in the CD45+ reference population is determined via flow cytometry, and the absolute CD4+ cell count is calculated (Claims 1, 2, 15-16). One of ordinary skill in the art would have been motivated to enumerate the number of CD4+ cells in a blood sample as a means for staging HIV-infected patients and monitoring the progression of the disease (See Pg. 328, col. 1). One would have expected success enumerating the number of CD4+ cells as the given cell subset in the dual platform method of Brando et al because enumeration of CD4+ cells by flow cytometry is well known and commonly practiced in the art; Brando et al do not alter the flow cytometry aspect of the method, but do provide teachings on using leukocytes as the reference cell population (See Pg. 330, col. 1).

Brando et al teach that the absolute cell count of the reference population can be obtained from the number of reference cells per volume of sample on a hematology analyzer (See pg. 329, col. 2-Pg. 330, col. 1); however they also teach that the number of cells per volume of sample can be obtained by microbead-based technologies. In microbead-based technologies known amounts of fluorescent microbeads are admixed with a known volume of stained blood in a lyse-no-wash technique and the beads are counted along with the cells, thus the number of cells per volume is obtained (See Pg. 334, col. 2). Therefore it would have been obvious to one of ordinary skill in the art to use either a hematology analyzer or microbead-based technologies to calculate the number of leukocyte reference cells in a sample

(Claims 14 & 16). One of ordinary skill in the art would have been motivated to use microbead-based technologies to obtain a reference cell count in order to eliminate errors due to variance between hematology analyzer technicians, as hematology analysis is performed by technicians and thus is subject to human error and variation between technicians' skill level (See Brando Pg. 330, col. 1 & Barnett et al, Pg. 1059, col. 1). One would have expected success using either cell counting method to obtain the absolute cell count of the reference cell population because Brando et al teach that both hematology analyzer and microbead-based technologies are acceptable cell counting methods.

It would further have been obvious to one of ordinary skill in the art to use any available blood sample to perform the analysis, including whole unlysed blood, unfractionated, fractionated or lysed whole blood (Claim 5). One of ordinary skill in the art would have been motivated to use any type of blood sample provided to perform the analysis because only the white blood cells are needed in the method. One of ordinary skill in the art would be motivated to use any type of blood sample in order to test the blood to monitor the progression of HIV in infected patients. Fractionating or lysing the blood sample would not affect the number of white blood cells or the CD4 or CD45 protein markers on the cells; therefore, one would expect success using any type of blood sample, based on what type of sample was provided, because a skilled technician would be able to identify and isolate the white blood cells from any type of blood sample and perform the method of Brando et al.

Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Initially it is noted that applicants enclosed several exhibits along with the response, some of which were cited within the discussion of unexpected results; however, the list of enclosures does not correlate to what was actually provided. Received were: (i) a single figure labeled "Exhibit 1" that

contained no explanation or discussion; (ii) a two page paper by Glencross entitled "Panleucogated (Plg) CD4 Counting: A Cost effective, simple and reproducible solution for HIV/AIDS monitoring in a resource limited setting" this was noted as the 'unpublished paper' referred to in the arguments, but this paper is only directed to the cost of different testing procedures, not to the method currently at hand; (iii) what appears to be a survey, headed "Name of Session: CD4+ T cell counting: affordable vs. comprehensive methods" the paper consisted only of questions and did not pertain to the method currently at hand; (iv) Mandy et al, MMWR Recommendations and Reports, 2003; (v) an abstract of Landay et al, Clin Immunol Immunopathol, 1989, which was cited in support of the argument against Melnicoff; and (vi) what does appear to be the unpublished paper of Glencross et al, entitled "Performance of PanLeucogated (PLG) CD4 lymphocyte enumeration: Cross platform equivalency, accuracy and reproducibility versus state of the art CD4 methods." Please note that appellants have the burden of explaining the data in any declaration they proffer as evidence of non-obviousness, because applicants failed to provide any direct explanation or discussion on the references, they have been considered only as far as they were deemed to pertain to the claimed invention. *Ex parte Ishizaka*, 24 USPQ2d 1621, 1624 (Bd. Pat. App. & Inter. 1992).

Applicant's arguments filed 12 December 2005 have been fully considered but they are not persuasive. Specifically applicant presents arguments against the art rejections over Melnicoff, Brando et al, and Barnett et al; applicant further argues that their method produces unexpected results compared to the standard method of using the total lymphocyte population as the reference population; finally applicant presents a list of awards and accomplishments of the inventor. For convenience, each of the arguments have been addressed below.

First, regarding the rejections over Melnicoff and Melnicoff in view of Brando, applicants argue that the Melnicoff reference inappropriately used the term "leukocytes" in example 3A in place of "lymphocytes" and thus Melnicoff is not an enabling disclosure for the use of the total leukocyte population as a means for enumerating the number of CD4+ lymphocytes in a blood sample. In support applicants state a review of Melnicoff makes it clear that a total lymphocyte count (not a total leukocyte count) was intended in the cited method. Applicants argue that Melnicoff et al claims a method of enumerating a subset of cells, such as CD4+ cells from blood sample, wherein their method does not rely on the total lymphocyte count (TLC); thus, applicants argue, because Melnicoff intends to claim a method different from the standard, they necessarily need to compare their method to the standard to show their unexpected results. Melnicoff explain the standard procedure in the art for enumerating CD4+ cells in a blood sample involves the following calculation: #CD4 lymphocytes per liter blood= (% CD4 lymphocytes)x(% lymphocytes in white blood cells)x(#white blood cells per liter blood) (See Melnicoff, col. 6, ln 13-15); Melnicoff also points out disadvantages and inaccuracies associated with use of the TLC. Applicants further point to a publication by Landay et al (only abstract provided) and a publication by the National Committee for Clinical Laboratory Standards (not provided) to show that the TLC is to be used in dual platform calculations, not the total leukocyte counts. Regarding use of Brando et al, applicants state that they do not remedy the deficiencies of Melnicoff.

In response, it is first noted that the abstract of the publication of Landay et al does not provide any teachings relevant to the current rejection, if the entire publication does contribute applicant must submit a complete copy along with an explanation of the evidence provided within; similarly, because the paper by the National Committee for Clinical Laboratory Standards was not provided, it has not been considered. However, the examiner does recognize that the total lymphocyte count (TLC) was considered the standard reference population for dual platform calculation of absolute CD4+ cells. Yet, while TLC may have been the standard, the reference must be taken for what is presented; example 3A of Melnicoff

clearly describes obtaining the total leukocyte count and obtaining the percent of leukocytes (CD45+) which are CD4+ lymphocytes (See Melnicoff, col. 19, ln 51-55 and col. 20, ln 15-24). While the applicants argue that Melnicoff intended to describe a step of determining the TLC (and not total leukocyte count) in order to create a standardized curve because such was the standard practice at the time, there is no clear statement in Melnicoff that they were trying to replicate the standard procedure at that time. In fact, Melnicoff had noted the problems using the total lymphocyte count, thus there is suggestion that they would have used an alternative method using the total leukocyte count as the reference population. Therefore, though Melnicoff varies from the standard practice at the time, it is merely speculation that they mischaracterized their method; thus the method provided by Melnicoff is interpreted as presented in the patent, and rejections based on Melnicoff stand.

Second, regarding the rejection over Brando et al in view of Barnett et al, applicants argue that the combination fails to recite each element of the present invention or provide an expectation of success. Specifically, applicants argue that Brando et al fails to disclose or suggest the direct use of a white cell count to derive an absolute CD4+ lymphocyte count. Applicants state Barnett et al fails to remedy the deficiencies.

In response, it is reiterated that Brando et al does in fact teach the total leukocyte population (white cell count) can be used as the reference population to derive an absolute count of subsets of blood cells; in particular Brando et al teach the pan-leukocyte CD45 marker can be used in the gating strategy to encompass all leukocytes (Se pg. 329, col. 2- Pg. 330, col. 2). Though Brando et al does not specifically teach enumerating the CD4+ cell population, reasoning has been provided to show why it would have been well within the purview of one of ordinary skill in the art at the time the invention was made to calculate the percentage of CD4+ cells in the total leukocyte population, see rejection of record.

Third, applicants submits that their gating method, described in claim 1, represents an improvement in the state of the art for both traditional dual and single platform methodologies, as it only typically requires total CD45++/total leukocyte expression, and is thus easier to use, is not affected by sample age, is more reliable and reproducible for both dual platform and single platform methods of CD4+ lymphocyte enumeration. Applicants point to the work of Mandy et al (2003), Barnett et al (1999), Schnizlein-Bick et al (2002, not provided), and Mandy et al (1997, not provided) to show unpopularity of dual platform methods which use the total lymphocyte counts (TLC). Applicants state their current method, which uses Dual platform PanLeucogating, uses a white blood cell count as opposed to TLC, and this significantly improves the reproducibility of traditional dual platform testing to equal levels, or superior results, compared to single platform bead methods. Applicants point to an unpublished paper by Glencross et al (provided) for support, but provide no specific discussion of the allegedly unexpected results discovered by Glencross et al.

In response, it is noted that applicant's arguments related to unexpected results continually point to the superiority of their Dual platform PanLeucogating method, however, the current claims do not recite any PanLeucogating method, in fact the claims do not even require flow cytometry; rather the current claims are directed to a broad method, void of specific steps, of CD4+ cell enumeration. The claimed method fails to describe a dual platform method or a single platform method of CD4+ cell enumeration, and thus it is unclear how the results of Glencross et al, which compare specific dual and single platform PanLeucogating strategies to conventional dual and single platform methods, are applicable to the claimed method. Specifically, the experiments of Glencross et al compare a dual platform PanLeucogating method, involving a first white blood cell count on a GenS or STKS hematology instrument, followed by analysis on an XL-MCL or FC500 Flow Cytometer with BC CXP software, wherein total leukocytes are identified on a CD45 vs. side scatter (SS) plot, and then CD4++ lymphoid cells are identified. Glencross et al presents what appears to be less intra- and inter-laboratory

difference in the results obtained using their method; however, there is no evidence to support applicants claims that their method is easier to use, is not affected by sample age, or that the results are more accurate/reliable. The currently claimed method does not provide the appropriate parameters or limitations to be considered commensurate in scope with the experimental evidence presented by Glencross et al; therefore, the results shown by Glencross et al are not applicable to the currently claimed method and the argument that the claimed method produces unexpected results is not persuasive. See *In re Clemens*, 622 F.2d 1029, 1036, 206 USPQ 289, 296 (CCPA 1980).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Allison M. Ford whose telephone number is 571-272-2936. The examiner can normally be reached on 7:30-5 M-Th, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Allison M Ford
Examiner
Art Unit 1651